

REMARKS

Support for the Claim Amendments

Applicants have amended claim 1 and added new claim 21. Support for the claim amendments can be found throughout the specification and originally filed claims. Specifically, paragraph 0068 of the published application (U.S. Pre-grant Publication No. 2007/1096336) and Example 1 support the claim amendments. Example 1 describes the construction of the T-BAC/Vec9 plasmid (see Figure 1), which was about 168.3 kb in length (157.7kb [T-BAC] + 10.569kb [pVec9]), prior to excision of the stuffer sequence. Paragraphs 0093-0099 of Example 1 describe the removal of the stuffer sequence (14.6kb) and the ability of the resulting virus to replicate. As one can see, the resulting genome was about 153.7kb in length (168.3kb [see above]-14.6kb [stuffer sequence]) and was still encapsulated in the viral capsid. One of skill in the art, therefore, would understand Example 1 as a descriptive illustration that the methods of the present invention can result in a viral genome that capable of being encapsulated in the viral capsid and is at least 150kb in length (after excision of the stuffer sequence). Accordingly, the specification fully supports the claim amendments.

The Claimed Invention is Not Obvious

The Office Action of 18 June 2009 rejected claims 1-4 and 5-9 as allegedly obvious in view of Chiocca (U.S. Published Application No. 2002/0110543), in view of Braeckfeld (U.S. Patent 6,573,090) and Saeki *et al.* (Mol. Ther. 3:591-601 (2001)). Applicants respectfully disagree. Applicants have nonetheless amended the claims to better capture the envisioned commercial embodiments and assert that the amendments to the claims render the obviousness rejection as moot. Specifically, Applicants have generated a recombinant herpes simplex virus containing a genetic construct that is greater than 150kb in length and the amended claims now reflect this specific embodiment. Applicants also offer the following comments.

The main argument that the Office Action sets forth is that the newly cited art, Braeckfeld, teaches “that BAC clones that comprise DNA that is more than 150kb in length can not package into viral capsids” According to the Office Action, therefore, one of skill would

read Braekefield and then recognize that any genetic construct that is more than 150kb would not be able to package in the capsid and thus could not be used to generate recombinant herpes simplex virus. Thus, Braekefield would cast serious doubt on the limits of the methods of Chiocca such that one of skill would have no reasonable expectation of success in combining Chiocca and Braekefield if the final genetic construct was 150kb or more.

In fact, Applicants assert that one of skill in the art would have an *a priori* expectation of failure in formulating the methods of the present invention after reading Braekefield. In the present invention, at least one of the resulting vectors generated was about 154kb in length. *See* Example 1. According to Braekefield, a DNA of this size would not be packaged. Thus one of skill in the art would actually expect failure with the presently claimed invention, based upon the combination of Chiocca and Braekefield. Based on this expectation of failure, Applicants assert that one of skill in the art would be motivated to avoid constructs of 150kb or greater.

To be clear, Applicants have generated a recombinant herpes simplex virus containing a genetic construct that is greater than 150kb in length. The fact that a herpes simplex virus is generated with the methods of the present invention indicates that the capsids are able to encapsulate the claimed genetic construct of more than 150kb. Applicants' generated recombinant virus is therefore opposite to what one of skill would expect after reading Chiocca and Braekefield.

Applicants assert that the combination of cited references, therefore, would not render obvious the claimed invention. First, the combination of references does not teach each and every element of the claims such that the resulting recombinant virus is at least 150kb. Second, there would be no expectation of success in generating a recombinant virus of more than 150kb. Finally, because there would actually be an expectation of failure, based on Braekefield, one of skill in the art would not be motivated to generate a recombinant virus of equal to or more than 150kb in length. Applicants respectfully request reconsideration and withdrawal of the obviousness rejection.

CONCLUSION

Applicants have amended the claim set to better capture the envisioned commercial embodiments and assert that these amendments render moot the remaining obvious rejections.

Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, he or she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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By /Todd B. Buck/

MORGAN LEWIS & BOCKIUS LLP

Customer Number: 09629

Telephone: (202) 739-3000

Facsimile: (202) 739-3001

Todd B. Buck

Registration No. 48,574